

20. (Amended) The composition of claim 8 wherein said osteochondral graft is osteochondral autograft.

21. (Amended) A composition for the regeneration of articular cartilage, said composition comprising an osteochondral graft having applied thereto an amount of BMP-2 effective for the regeneration of said articular cartilage.

### REMARKS

Applicants have cancelled claims 2, 4, 5, 9, 11, 12, 15, and 18, without prejudice to their right to prosecute these claims in a later filed application. Claims 1, 6, 7, 8, 10, 13, 14, 16, 17, 19, 20, and 21 have been amended. The pending claims are directed to processes for the regeneration of articular cartilage comprising administration of an osteochondral graft having an effective amount of a BMP applied to it and compositions comprising an osteochondral graft having an effective amount of a BMP applied to it. Claims 6, 7, 13, and 14 have also been amended to render the language of the claims more precise. Applicants submit that no new matter has been added by these amendments nor do the amendments raise new issues or necessitate the undertaking of any additional search of the art by the Examiner. All elements now claimed were either previously claimed or inherent in the claims as examined. An appendix showing the changes made to the claims is attached.

### REJECTIONS UNDER 35 U.S.C. §112

Pending claims 6, 7, 13, 14, 16, and 17 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Claims 6, 7, 13, and 14 have been amended to replace the phrase "ligament-like tissue" with "ligament" as suggested by the

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Examiner to overcome the rejection. Claims 7 and 14 have been amended to insert a comma after BMP-13, thereby overcoming the basis for the rejection of these claims. In view of these amendments, Applicants request that the rejections under 35 U.S.C. § 112, second paragraph, be withdrawn.

#### **REJECTIONS UNDER 35 USC §102**

Claims 1, 3, 6-8, 10, 13, and 14 stand rejected under §102(b) as allegedly anticipated by Hattersley *et al.* (U.S. Patent No. 5,700,744). Claims 1, 6-8, 13, and 14 stand rejected as allegedly anticipated by Celeste *et al.* (U.S. Patent No. 5,658,882). Applicants traverse.

As noted above, the pending claims are directed to processes for the regeneration of articular cartilage comprising administration of an osteochondral graft having an effective amount of a BMP applied to it and compositions comprising an osteochondral graft having an effective amount of a BMP applied to it. Neither Hattersley *et al.* (as acknowledged by the Examiner at page 7 of the Office Action) nor Celeste *et al.* teach or suggest an osteochondral graft having BMP applied to it for the regeneration of articular cartilage. Therefore, none of the pending claims are anticipated by Hattersley *et al.* or Celeste *et al.* and Applicants request that the rejections under 35 U.S.C. § 102 be withdrawn.

#### **REJECTION UNDER 35 USC §103**

The claims stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Hattersley *et al.* (U.S. Patent No. 5,700,774) in view of Nevo *et al.* (U.S. Patent No. 4,642,120). The Examiner alleges that Nevo *et al.* teaches the use of osteochondral grafts in association with articular cartilage damage and that it would have been obvious

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to one of ordinary skill in the art to have modified Hattersley *et al.* by using the teaching of Nevo *et al.* The Examiner concludes that the claimed invention was within the ordinary skill in the art to make and use at the time it was made and thus, was as a whole, *prima facie* obvious.

Applicants respectfully disagree with the Examiner's analysis and submit that the claimed invention is not rendered obvious by the combination of Hattersely *et al.* and Nevo *et al.* for one very simple reason. Nevo *et al.* does not teach the use of osteochondral grafts in association with articular cartilage damage. In fact, Nevo *et al.* teaches away from the use of osteochondral grafts. At column 1, lines 35-38, Nevo *et al.* states "various attempts have been made to resort to osteochondral grafts and to the provision of various forms of prosthesis, but long-term results have been poor and discouraging." Instead Nevo *et al.* teaches the use of compositions for articular cartilage repair that comprise cells such as embryonal chondrocytes, mesenchymal cells, or bone marrow stem cells -- all of which can be converted to cartilage by the influence of chondrogenic-inducing factors - in a biological milieu which forms a "gel." The claimed invention requires osteochondral graft, which relies on the presence of both cartilage and bone tissue. This feature is not described or suggested by either Hattersely *et al.* or Nevo *et al.* In short, the combination of references fails to teach or suggest an osteochondral graft having applied thereto an effect amount of BMP for the regeneration of articular cartilage. Thus, the rejection under 35 U.S.C. § 103 cannot be maintained.

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In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

Applicants believe that any extension of time required for entry of this Amendment is accounted for in the accompanying Petition for Extension of Time. However, in the event of an error, please grant any additional extensions of time required to enter the Amendment and charge any additional required fees to deposit account 06-0916.

Respectfully submitted,

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**APPENDIX TO AMENDMENT OF SHOWING CHANGES MADE TO CLAIMS**

Claims 2, 4, 5, 9, 11, 12, 15, and 18 have been cancelled.

Claims 1, 6, 7, 8, 10, 13, 14, 16, 17, 19, 20, and 21 have been amended as follows:

1. (Amended) A method for regeneration of articular cartilage comprising administering to an area in need of regeneration of said articular cartilage an osteochondral graft having applied thereto ~~an effective amount~~ of at least one purified bone morphogenetic protein (BMP) effective for the regeneration of said articular cartilage.

6. (Amended) The method of claim 1 further comprising a protein which induces the formation of tendon or ligament-like tissue.

7. (Amended) The method of claim 6 wherein said protein which induces the formation of tendon or ligament-like tissue is selected from the group consisting of BMP-12, BMP-13<sub>1</sub>, members of the BMP-12 subfamily<sub>1</sub>, and MP52.

8. (Amended) A composition for regeneration of articular cartilage comprising an osteochondral graft having applied thereto ~~an effective amount~~ of at least one purified bone morphogenetic protein (BMP) effective for the regeneration of said articular cartilage.

10. (Amended) The composition of claim 4-8 wherein said BMP is BMP-2.

13. (Amended) The composition of claim 4-8 further comprising a protein which induces the formation of tendon or ligament-like tissue.

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14. (Amended) The composition of claim ~~6~~8 wherein said protein which induces the formation of tendon or ligament-like tissue is selected from the group consisting of BMP-12, BMP-13, members of the BMP-12 subfamily, and MP52.

16. (Amended) The method of claim ~~15~~1 wherein said osteochondral graft is osteochondral allograft.

17. (Amended) The method of claim ~~15~~1 wherein said osteochondral graft is osteochondral autograft.

19. (Amended) The composition of claim ~~18~~8 wherein said osteochondral graft is osteochondral allograft.

20. (Amended) The composition of claim ~~18~~8 wherein said osteochondral graft is osteochondral autograft.

21. (Amended) A composition for the regeneration of articular cartilage said composition comprising an osteochondral graft having applied thereto an effective  
~~amount of an osteochondral graft in combination with an effective~~ amount of BMP-2  
effective for the regeneration of said articular cartilage.